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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/129,758	Applicant(s) WALDMANN et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 5, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 5, 11-13, 15, 17-24, and 26-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 5, 11-13, 15, 17-24, and 26-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amendment filed 11/12/02 has been entered (paper number 20). Priority papers filed 12/5/02 have been entered (paper number 22). Applicant has amended claims 1-3, 5, 11-13, 15, 17-24, 26-29.

Objections

2. The disclosure remains objected to because of the following informalities: Applicants are required to use the heading "Brief Description of the Drawings" to describe the drawings. See MPEP 608.01(f). Applicant has used "BRIEF DESCRIPTION OF THE SEQUENCES AND DRAWINGS".

Claim Rejection, 35 U.S.C. 112

3. Amended claims 1-3, 5 11-13, 15, 17-24 and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 11 are indefinite because the name mammalian neuronal cationic ASIC channel does not provide any structural limitation on the claim and the metes and bounds of the claim cannot be determined. Applicant has amended the claim by inserting "ASIC". The inclusion of "ASIC" does not provide any information as to the structure of the claimed invention.

Claims 2, 3, 5 remain indefinite because it is not clear what is a "functionally equivalent derivative" so as to allow the metes and bounds of the claim to be determined. Applicant argues

a definition of the term "functionally equivalent derivative" is provided on page 2 of the specification and specific examples are set forth proceeding into page 3. Applicants arguments have been fully considered but not found persuasive. The specification, does not provide a clear definition of the term "functionally equivalent derivative". The specification, on page 2, discloses "Such derivatives are those whose sequence includes a modification and/or suppression and/or an addition of one or more amino acid residues. As long as this modification and/or suppression and/or addition does not modify the functional and structural properties of the ASIC channel, principally its activation by protons". The definition provides no structure of the claimed derivatives. The definition does not disclose the specific modifications or suppressions or additions. Further the specific function and structural properties of the derivative are not disclosed. Also it is not clear what else is included or excluded by the functional term "principally its activation by protons". Although examples of "functionally equivalent derivative" are provided they do not provide a definition of the term so as to allow the metes and bounds of the claim to be determined. It is not clear what "functionally equivalent derivative" includes and exclude. The terms "derivative" carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules.

Claim 21 recites the limitation "the mammalian neuronal amiloride-sensitive proton-activated cationic channels" in claim 18. There is insufficient antecedent basis for this limitation in the claim. Claim 18 nor any of the base claims from which claim 18 depends recite the term "the mammalian neuronal amiloride-sensitive proton-activated cationic channels". Further claim

21 is indefinite because a transformed cell cannot be obtained by the method according to claim 18. Claim 18 is directed to a method for producing a protein.

Claim 22 is indefinite because the method steps do not achieve the goal of screening a substance capable of modulating activity of mammalian neuronal cationic channels as stated in the preamble. The "selected value" which determines when the goal of the claim is achieved has not been disclosed. Also, it is not clear if the method screens for cationic channels or some other channels that may be present in the cell. The method as presently claimed does not limit the screening to specific neuronal channels. The current change may be result of the modulation of some channel protein which was inherently present in the cell before transformation as claimed in claim 21.

Claim 28 is indefinite because the method steps do not achieve the goal of screening a substance capable of modulating activity of mammalian neuronal cationic channels as stated in the preamble. The "selected value" which determines when the goal of the claim is achieved has not been disclosed. Also, it is not clear if the method screens for cationic channels or some other channels that may be present in the cell. The method as presently claimed does not limit the screening to specific neuronal channels. The current change may be result of the modulation of some channel protein which was inherently present in the cell before transformation as claimed in claim 27.

Claims 26 is an improper Markush grouping encompassing both a genus and a species. Further the claim is not in the proper format for a Markush claim. The claim should be written in a format such as "----wherein the host cell is selected from the group consisting of A, B, C and D". It is not clear when the host cell should be "notably" selected.

Claim 27 recites the limitation "the mammalian neuronal amiloride-sensitive proton-activated cationic channels" in claim 19. There is insufficient antecedent basis for this limitation in the claim. Claim 19 nor any of the base claims from which claim 19 depends recite the term "the mammalian neuronal amiloride-sensitive proton-activated cationic channels". Further claim 27 is indefinite because a transformed cell cannot be obtained by the method according to claim 19. Claim 19 is directed to a method for expressing a protein.

Claims 12-13, 15, 1720, 23, 24 and 29 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Amended claims 1-3, 5 11-13, 15 and 17-24 and 26-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicant argues the ASIC channels of instant invention are useful for screening substances capable of modulating the perception of acidity regarding both noiception and taste transduction, said substances being further useful in the fabrication of drugs intended for the treatment or prevention of pathologies entailing the painful perception of acidity which interferes in inflamationory diseases, ischemias and selected tumors. Applicant also argues the nucleic acid encoding ASIC channel may be used to produce transgenic animals. Applicant further disclose that utility is confirmed due : the disclosure of ASIC1 knockout mouse by Wemmie which display defective spatial learning and eyeblink conditioning, b) Violley disclosing that ASIC subunits are up-regulated during the inflammation and that ASIC might be a target for nonsterioid anti-inflammatory drugs, c) disclosure of Price that inactivation of ASIC3 causes altered mechanosensation and acid evoked noiception, d) disclosure of Chen that shows that inactivation of ASIC3 causes noiception, e) disclosure of Sutherland that suggests ASIC3 might play an important role in the perception of pain during cardiac ischemia. Applicants arguments have been fully considered but not found persuasive. The finding of the post filing art, relied on by applicant to argue utility, were not disclosed in instant application. Therefore, said post filing art cannot be used to support utility in instant application. Also it is not clear which reference contains the protein of SEQ ID NO:2, 4, or 8. Applicant is requested to clarify

which of the references cited in paper number 20 refer to the ion channel identified by SEQ ID NOs:2 , 4 or 8 . The protein gated channel of instant invention belongs to a complex family of ion channels with varied properties and functions ranging from spatial learning, eyeblink condition, perception of pain and perception of acidity. The specification discloses, pages 2 and 3, the family of structural relatives of ASIC channels (also designated as MDEG) have different electrophysiological properties and that no normal physiological function of said MDEG was known until the demonstration of its activation by protons (also see page 17, lines 13-16). Also disclosed, page 5, inactivation and kinetics and the ionic selectivity of the channel formed after co-expression of different MDEG are different than those if only one channel is expressed. The specification, page 5, lines 8-9 states, when referring to claimed invention, "this property is very similar to that of the proton-activated cationic channel which is implicated in the prolonged sensation of pain caused by acidosis. It is very probable that DRASIC and MDEG2 are part of this channel". The claimed ion channel is speculated to be similar to the family of proton-activated ion channels, but there is no disclosure in the specification that instant invention is useful for screening substances capable of modulating the perception of acidity regarding both noiception and taste transduction, said substances being further useful in the fabrication of drugs intended for the treatment or prevention of pathologies entailing the painful perception of acidity which interferes in inflamationory diseases, ischemias and selected tumors. The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the ion channel of the instant invention. The disclosed

protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 1-3, 5, 11-13, 15, 17-24 and 26-29. The claims are directed to: a) isolated nucleic acid comprising a sequence that encodes a cation channel b) Protein comprising a cation channel protein and methods of screening substances that are capable of modulating the activity of the ion channel. Claims are also directed to cell transfected with the claimed nucleic acid.

The specification discloses a the protein of SEQ ID NOs:2, 4 and 8 encoded by the nucleic acid of SEQ ID NOs:1, 3 and 7. The specification discloses, page 3, lines 4-7, "no normal physiological function of MDEG was known until the demonstration of its activation by protons in accordance with cationic channels of the present invention.

The specification discloses general functional activities of cationic channels but does not disclose any activity associated with the claimed cationic channel. In light of the specification the skilled artisan can conclude that protein of instant invention is a cationic channel protein. However, no disclosure is provided within the instant specification on what specific function the claimed cationic channel protein possesses, nor are any disease states disclosed that are directly related to cation channel dysfunction. Ions are known to play a role of first or second messenger in numerous cellular signaling contexts, but it is not known what role claimed cationic channel plays signaling and what would be the use of interfering with its function, apart from as targets for drug discovery

The utilities asserted by Applicant are not specific or substantial. Since no specific function of claimed cation channel is known, and the ability to transport ions with no associated function is not considered a "well established utility" the hypothesized functions are based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the nucleic acid of SEQ ID NO:1, 3 or 8 encoding the protein of SEQ ID NO:2, 4 or 8 or fragments thereof useful to identify drugs that affect said protein and modulate

its activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity of claimed cation channel. Thus the corresponding asserted utilities are essentially methods of using claimed cation channel to identify or treat disease states associated with cation channel polypeptide disfunction and as targets for drug discovery. Therefor the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with claimed cation channel, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed cation channel, further experimentation is necessary to attribute a utility to the claimed cation channel. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the reason given above and the claims are rejected. Likewise cells transfected with claimed nucleic acid, and methods of screening using claimed cation channel, lack utility for these reasons given above.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

Claims of instant invention are drawn to the use of a polypeptide or nucleic acid encoding said polypeptide with, as yet, undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO:2, 4 or 8 or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to other ion channel proteins based on sequence similarity. As disclosed by above, the family of proteins related to instant invention may have diverse effects and bind a diverse number of ligands. Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for proteins of SEQ ID NO:2, 4 or 8, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

5. Amended 1-3, 5 11-13, 15, 17-24 and 26-29 rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed cation channel, further experimentation is necessary to attribute a utility to the claimed polypeptides, polynucleotides and methods of their use. The rejection is essential the same as in paper number 18, but is included to address the claims as amended.

While the person of ordinary skill in the art would, in light of the specification be able to isolate polypeptides represented by SEQ ID NOS: 2, 4 and 8 encoded by the nucleic acid of SEQ ID NOs:1, 3 and 7, respectively, the scope of the claims, which encompass polypeptides and polynucleotides with no defined structure and function which encompasses, mutants, variants, analogs, homologs or derivatives of SEQ ID NOS:2, 4 and 8 are not enabled by the disclosure. The disclosure does not teach how to make functional mutants, variants, analogs, homologs or derivatives of SEQ ID NOS:2, 4 and 8, or to use a commensurate number of the inactive fragments, mutants, variants, analogs, homologs or derivatives which may be structurally and functionally different to the disclosed proteins of SEQ ID NOs:2, 4 and 8. There is no disclosure of the critical structural feature of the invention or how it relates structure to function. Due to the large quantity of experimentation necessary to identify the polypeptides and polynucleotides of instant invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:2, 4 and 8 are also encompassed by the claims), and the breadth of the claim which fail to recite structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope. Further the name "mammalian ASIC neuronal cation channel provides no structure to the claimed protein.

While the person of ordinary skill in the art, would, in light of the specification, be able to make polypeptides of SEQ. ID. NO:2, SEQ ID 4 and SEQ ID NO:8, the scope of the claims, which encompass any polypeptide and polynucleotide which can be loosely classified as an mammalian ASIC neuronal cationic channel, is simply not enabled by the disclosure. The disclosure does not teach how to use any of the numerous polypeptides or variants, which are encompassed by the claims, but are inactive or lack functionality.

Further mammalian neuronal cationic channel or functionally equivalent derivative also fails to identify polypeptide or its encoded of polypeptide by specific functional activity or specific structure. The claims encompass compounds whose scope cannot be determined due to indefiniteness of the claims (see rejection, above) . Further, structural features that could distinguish the compounds in the genus from others are missing from the disclosure. There is no disclosure of the critical technical feature of the invention. The prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered, nor does the specification provide any guidance as to how the skilled artisan could use an inactive variants, mutants. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that variants and mutants could be used for any purpose. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to make, isolate,

identify and use the claimed variant nucleic acid encoding polypeptides encompassed, without undue experimentation.

Therefore, due to the lack of direction/guidance presented in the specification regarding the production, identification, purification, isolation and characterization of the mutants, variants, analogs, homologs or derivatives of SEQ ID NOS:2, 4 and 8, encompassed by the claims, the unpredictability of the effects of mutation on the structure and function of proteins, and the breadth of the claim which fail to recite specific structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention. Further since the compounds of SEQ D Nos 1-4 and 7-8 and their derivatives are not enabled for the reasons given above, methods of using said compounds is also not enabled.

Claim 24 remains rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the claimed pharmaceutical composition. Applicant has not provided specific arguments to stated rejection. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specification provides no guidance on the function of the polypeptide of SEQ ID NO:2, 4 and 8 or derivative thereof. The specification nor prior art disclose any disease states containing an abnormality involving the compounds of SEQ ID NOs:1-4 and 7-8. The specification nor prior art suggest that administration of the afore mentioned compounds would be beneficial as

treatment or even if the pharmaceutical composition would reach its target without being degraded. Further said compositions could be toxic.

While the person of ordinary skill in the art would, in light of the specification be able to make composition containing the claimed compounds, the scope of the claims, which encompass pharmaceutical composition is not enabled by the disclosure. The disclosure does not teach how to make functional derivatives of the claimed compounds and how to use pharmaceutical compositions which were not effective in the treatment. Due to the large quantity of experimentation necessary to identify the derivatives and the compounds of SEQ ID NOS:1-4 and 7-8 that can treat specific diseases, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said compounds as relate to treatment of disease states(would these compounds increase or decrease a particular activity related to a disease state) , the unpredictability of the effects of the afore mentioned agents on the disease state and the breadth of the claim which fail to recite specific structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention.

6. Amended claims 1-3, 5, 11, 17, 18-24 and 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in

sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. The rejection is essentially the same as in paper number 18, but is recast below to address the amended claims. Applicant has not provided any specific arguments to the rejections under 35 U.S.C. 112, first paragraph, written description. The claims are directed to the compounds of SEQ ID NOs:1-4 and 7-6, their derivatives and methods of their use.

The specification discloses the polypeptide of SEQ ID NO:2, 4 and 8 encoded by the polynucleotide of SEQ ID NO:s 1, 3 and 7. The instant disclosure of three distinct polypeptide does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length, truncated, fusion molecules and variants thereof; A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by an amino acid sequence, falling within the scope of the genus or of a recitation of structural and functional features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides and polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The fusion polypeptides, fragments and variants encompassed by the claims do not disclose the critical technical feature of the claimed invention or its relationship to

function. For example, polypeptides comprising a fragment or variants of SEQ ID NO:2, 4 and 8 may be completely unrelated to the disclosed polypeptide of SEQ ID NO: 2, 4 and 8, having a different function or even be inactive. The critical technical feature encompassed by the fragments and variants must relate to the encompassed polypeptide, structurally and functionally to the disclosed proteins of SEQ ID NO:2, 4 and 8. The same argument applies to the mutants, variants, analogs, homologs, derivatives and fusion products encompassed by the claims. It is not clear what critical technical feature undisclosed amino acids, disclosed amino acids in a specific fragment, or recited descriptive language provide so as to show a written description of the invention in full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. There is no description, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the encoded polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the regulatory regions essential to the function of the claimed invention, which are required since the claimed invention currently

encompasses the full length, truncated, fusion products and variants thereof. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus may be highly variant, the disclosure is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

An adequate written description of a protein or nucleic acid molecule requires a precise definition, such as by structure, formula, chemical name, and physical properties, not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, an adequate written description of a polypeptide is more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polynucleotide or the encoded protein itself. Accordingly, the specification does not provide a written description of the invention of claims 1-3, 5, 11, 17, 18-24 and 26-29

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, **there is no clear evidence of activity possessed by the**

claimed genus of polypeptides, the critical special technical feature of the polypeptides or how the critical special technical feature encompassed by the genus claimed relates to function. Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the variants of the polypeptide of SEQ ID NO:2, 4 and 15 have the same activity as the protein of SEQ ID NO:2, 4 and 8, since no activity is disclosed, nor the fragments disclosed with the critical special technical feature of the invention. The breadth of the claim come from encompassing polynucleotide encoding a protein, the fragments or variants which do not have an associated structure which defines the critical special technical feature of the invention. Further claim 1 does not even provide any structural information about the claimed polypeptide but claims every protein that is sensitive to amiloride.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is

required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

With the exception of SEQ ID NO:2, 4 and 8, the skilled artisan cannot envision the detailed chemical structure of the claimed polypeptide and polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not achieved. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class.

Therefore, only the polypeptide comprising SEQ ID NO:2, 4 and 8, the nucleic acid comprising SEQ ID Nos: 1, 3 and 7, vectors containing said nucleic acid, cells containing said vector and methods using said polypeptide, nucleic acid, vector, cell but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115). Methods for using derivatives, mutants and variants of SEQ ID NOs:1-4 and 7-8 also do not meet written description for the reasons given above.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
February 8, 2003

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